

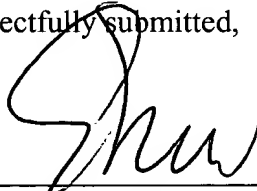
### REMARKS

The present amendment was made to correct multiple dependencies and to clarify the invention. Support for new claims 433-444 can be found in the application as originally filed. See the specification, for instance, at page 77 (whole page) to page 79, line 10. Claims 243-265, 267, 291-336, 360-406, 422, 426, 428, 430, and 432-444 are pending in this case. No new matter has been added to the application as a result of the present amendment.

Prompt consideration and entry of this amendment prior to examination is respectfully requested. The Commissioner is authorized to deduct any fees associated with this amendment from Deposit Account No. 13-2490.

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Respectfully submitted,

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**APPENDIX A**  
(clean copy of all pending claims)

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243. Nanoparticles having oligonucleotides attached to them, the oligonucleotides comprising at least one type of recognition oligonucleotides, each of the recognition oligonucleotides comprising a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least one portion of the sequence of a nucleic acid or another oligonucleotide.

244. The nanoparticles of Claim 243 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

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245. The nanoparticles of Claim 243 wherein the spacer portion comprises at least about 10 nucleotides.

246. The nanoparticles of Claim 245 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

247. The nanoparticles of Claim 243 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

248. The nanoparticles of Claim 243 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm<sup>2</sup>.

249. The nanoparticles of Claim 248 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm<sup>2</sup>.

250. The nanoparticles of Claim 249 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm<sup>2</sup> to about 40 picomoles/cm<sup>2</sup>.

251. The nanoparticles of Claim 243 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

252. The method of Claim 251 wherein the nanoparticles are gold nanoparticles.

253. (Amended) Nanoparticles having oligonucleotides attached to them, the oligonucleotides comprising: (a) at least one type of recognition oligonucleotides, each of the types of recognition oligonucleotides comprising a sequence complementary to at least one portion of the sequence of a nucleic acid or another oligonucleotide; and (b) a type of diluent oligonucleotides.

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254. The nanoparticles of Claim 253 wherein, each of the recognition oligonucleotides comprises a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least one portion of the sequence of a nucleic acid or another oligonucleotide.

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255. The nanoparticles of Claim 254 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

256. The nanoparticles of Claim 254 wherein the spacer portion comprises at least about 10 nucleotides.

257. The nanoparticles of Claim 256 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

258. The nanoparticles of Claim 254 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

259. The nanoparticles of Claim 253 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm<sup>2</sup>.

260. The nanoparticles of Claim 259 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm<sup>2</sup>.

261. The nanoparticles of Claim 260 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm<sup>2</sup> to about 40 picomoles/cm<sup>2</sup>.

262. The nanoparticles of Claim 254 wherein the diluent oligonucleotides contain about the same number of nucleotides as are contained in the spacer portions of the recognition oligonucleotides.

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263. The nanoparticles of Claim 262 wherein the sequence of the diluent oligonucleotides is the same as that of the spacer portions of the recognition oligonucleotides.

cont'd  
264. The nanoparticles of Claim 253 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

265. The nanoparticles of Claim 264 wherein the nanoparticles are gold nanoparticles.

267. (Amended) A method of detecting a nucleic acid comprising:  
contacting the nucleic acid with at least one type of nanoparticles according to any one of Claims 243 or 253 under conditions effective to allow hybridization of at least one of the types of recognition oligonucleotides on the nanoparticles with the nucleic acid; and  
observing a detectable change brought about by hybridization of the recognition oligonucleotides with the nucleic acid.

291. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles according to any one of Claims 243 or 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on each nanoparticle comprising a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

292. (Amended) A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles according to Claim 243 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to a first portion of the sequence of the nucleic acid, the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

293. The method of Claim 292 wherein the contacting conditions include freezing and thawing.

294. The method of Claim 292 wherein the contacting conditions include heating.

295. The method of Claim 292 wherein the detectable change is observed on a solid surface.

296. The method of Claim 292 wherein the detectable change is a color change observable with the naked eye.

297. The method of Claim 296 wherein the color change is observed on a solid surface.

298. The method of Claim 292 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

299. The method of Claim 298 wherein the nanoparticles are made of gold.

300. The method of Claim 292 wherein the recognition oligonucleotides attached to the nanoparticles are labeled on their ends not attached to the nanoparticles with molecules that produce a detectable change upon hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

301. The method of Claim 300 wherein the nanoparticles are metallic or semiconductor nanoparticles and the oligonucleotides attached to the nanoparticles are labeled with fluorescent molecules.

302. The method of Claim 292 wherein:  
the nucleic acid has a third portion located between the first and second portions, and the sequences of the oligonucleotides on the nanoparticles do not include sequences complementary to this third portion of the nucleic acid; and

the nucleic acid is further contacted with a filler oligonucleotide having a sequence complementary to this third portion of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the filler oligonucleotide with the nucleic acid.

303. The method of Claim 292 wherein the nucleic acid is viral RNA or DNA.

304. The method of Claim 292 wherein the nucleic acid is a gene associated with a disease.

305. The method of Claim 292 wherein the nucleic acid is a bacterial DNA.

B1 306. The method of Claim 292 wherein the nucleic acid is a fungal DNA.

307. The method of Claim 292 wherein the nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

cont'd 308. The method of Claim 292 wherein the nucleic acid is from a biological source.

309. The method of Claim 292 wherein the nucleic acid is a product of a polymerase chain reaction amplification.

310. The method of Claim 292 wherein the nucleic acid is contacted with the first and second types of nanoparticles simultaneously.

311. The method of Claim 292 wherein the nucleic acid is contacted and hybridized with the oligonucleotides on the first type of nanoparticles before being contacted with the second type of nanoparticles.

312. The method of Claim 311 wherein the first type of nanoparticles is attached to a substrate.

313. The method of Claim 292 wherein the nucleic acid is double-stranded and hybridization with the oligonucleotides on the nanoparticles results in the production of a triple-stranded complex.

314. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles according to Claim 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on each nanoparticle comprising a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

315. (Amended) A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles according to Claim 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to a first portion of the sequence of the nucleic acid, the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

316. The method of Claim 315 wherein the contacting conditions include freezing and thawing.

317. The method of Claim 315 wherein the contacting conditions include heating.

318. The method of Claim 315 wherein the detectable change is observed on a solid surface.



319. The method of Claim 315 wherein the detectable change is a color change observable with the naked eye.

320. The method of Claim 319 wherein the color change is observed on a solid surface.

B/ 321. The method of Claim 315 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

322. The method of Claim 321 wherein the nanoparticles are made of gold.

continued 323. The method of Claim 315 wherein the recognition oligonucleotides attached to the nanoparticles are labeled on their ends not attached to the nanoparticles with molecules that produce a detectable change upon hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

324. The method of Claim 323 wherein the nanoparticles are metallic or semiconductor nanoparticles and the recognition oligonucleotides attached to the nanoparticles are labeled with fluorescent molecules.

325. The method of Claim 315 wherein:  
the nucleic acid has a third portion located between the first and second portions, and the sequences of the oligonucleotides on the nanoparticles do not include sequences complementary to this third portion of the nucleic acid; and

the nucleic acid is further contacted with a filler oligonucleotide having a sequence complementary to this third portion of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the filler oligonucleotide with the nucleic acid.

326. The method of Claim 315 wherein the nucleic acid is viral RNA or DNA.

327. The method of Claim 315 wherein the nucleic acid is a gene associated with a disease.

328. The method of Claim 315 wherein the nucleic acid is a bacterial DNA.

329. The method of Claim 315 wherein the nucleic acid is a fungal DNA.

330. The method of Claim 315 wherein the nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

331. The method of Claim 315 wherein the nucleic acid is from a biological source.

332. The method of Claim 315 wherein the nucleic acid is a product of a polymerase chain reaction amplification.

333. The method of Claim 315 wherein the nucleic acid is contacted with the first and second types of nanoparticles simultaneously.

334. The method of Claim 315 wherein the nucleic acid is contacted and hybridized with the recognition oligonucleotides on the first type of nanoparticles before being contacted with the second type of nanoparticles.

335. The method of Claim 334 wherein the first type of nanoparticles is attached to a substrate.

336. The method of Claim 315 wherein the nucleic acid is double-stranded and hybridization with the oligonucleotides on the nanoparticles results in the production of a triple-stranded complex.

360. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

(a) contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;

(b) contacting said nucleic acid bound to the substrate with a first type of nanoparticles according to Claim 243 having one or more types of recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides comprising a sequence complementary to a second portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with said nucleic acid; and

(c) observing a detectable change.

361. (Amended) The method of Claim 360 further comprising:

(d) contacting the first type of nanoparticles bound to the substrate with a second type of nanoparticles according to Claim 243 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(e) observing the detectable change.

362. The method of Claim 360 wherein at least one of the types of recognition oligonucleotides on the first type of nanoparticles has a sequence complementary to the sequence of at least one of the types of oligonucleotides on the second type of nanoparticles and the method further comprises:

(f) contacting the second type of nanoparticles bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(g) observing the detectable change.

363. The method of Claim 362 wherein step (d) or steps (d) and (f) are repeated one or more times and the detectable change is observed.

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364. (Amended) The method of Claim 360 further comprising:

(d) providing a type of binding oligonucleotides having a sequence comprising at least two portions, the first portion being complementary to at least one of the types of oligonucleotides on the first type of nanoparticles;

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(e) contacting the binding oligonucleotides with the first type of nanoparticles bound to the substrate, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the first type of nanoparticles;

(f) providing a second type of nanoparticles according to Claim 243 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the second portion of the sequence of the binding oligonucleotides;

(g) contacting the binding oligonucleotides bound to the substrate with the second type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the binding oligonucleotides; and

(h) observing the detectable change.

365. The method of Claim 364 further comprising:

(i) contacting the second type of nanoparticles bound to the substrate with the binding oligonucleotides, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the second type of nanoparticles;

(j) contacting the binding oligonucleotides bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow

hybridization of the oligonucleotides on the first type of nanoparticles with the binding oligonucleotides; and

(k) observing the detectable change.

366. The method of Claim 365 wherein steps (e) and (g) or steps (e), (g), (i) and (j) are repeated one or more times, and the detectable change is observed.

367. The method of Claim 360 wherein the substrate is a transparent substrate or an opaque white substrate.

368. The method of Claim 367 wherein the detectable change is the formation of dark areas on the substrate.

369. The method of Claim 360 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

370. The method of Claim 369 wherein the nanoparticles are made of gold or silver.

371. The method of Claim 360 wherein the substrate has a plurality of types of oligonucleotides attached to it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

372. The method of Claim 360 wherein the substrate is contacted with silver stain to produce the detectable change.

373. The method of Claim 371 wherein the substrate is contacted with silver stain to produce the detectable change.

375. The method of Claim 360 wherein the detectable change is observed with an optical scanner.

376. The method of Claim 375 wherein the device is a flatbed scanner.

377. The method of Claim 375 wherein the scanner is linked to a computer loaded with software capable of calculating greyscale measurements, and the greyscale measurements are calculated. to provide a quantitative measure of the amount of nucleic acid detected.

378. The method of Claim 360 wherein the oligonucleotides attached to the substrate are located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

379. The method of Claim 378 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

380. The method of Claim 378 wherein the substrate is contacted with silver stain to produce the change in conductivity.

381. The method of Claim 371 wherein each of the plurality of oligonucleotides attached to the substrate in the array is located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

382. The method of Claim 381 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

383. The method of Claim 381 wherein the substrate is contacted with silver stain to produce the change in conductivity.

384. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

(a) contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence

of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;

(b) contacting said nucleic acid bound to the substrate with a first type of nanoparticles according to Claim 253 having one or more types of recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides comprising a sequence complementary to a second portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with said nucleic acid; and

(c) observing a detectable change.

385. (Amended) The method of Claim 384 further comprising:

(d) contacting the first type of nanoparticles bound to the substrate with a second type of nanoparticles according to Claim 253 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(e) observing the detectable change.

386. The method of Claim 385 wherein at least one of the types of recognition oligonucleotides on the first type of nanoparticles comprises a sequence complementary to the sequence of at least one of the types of oligonucleotides on the second type of nanoparticles and the method further comprises:

(f) contacting the second type of nanoparticles bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(g) observing the detectable change.

387. The method of Claim 386 wherein step (d) or steps (d) and (f) are repeated one or more times and the detectable change is observed.

388. (Amended) The method of Claim 384 further comprising:

(d) providing a type of binding oligonucleotides having a sequence comprising at least two portions, the first portion being complementary to at least one of the types of oligonucleotides on the first type of nanoparticles;

(e) contacting the binding oligonucleotides with the first type of nanoparticles bound to the substrate, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the first type of nanoparticles;

(f) providing a second type of nanoparticles according to Claim 253 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the second portion of the sequence of the binding oligonucleotides;

(g) contacting the binding oligonucleotides bound to the substrate with the second type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the binding oligonucleotides; and

(h) observing the detectable change.

389. The method of Claim 388 further comprising:

(i) contacting the second type of nanoparticles bound to the substrate with the binding oligonucleotides, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the second type of nanoparticles;

(j) contacting the binding oligonucleotides bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first type of nanoparticles with the binding oligonucleotides; and

(k) observing the detectable change.



390. The method of Claim 389 wherein steps (e) and (g) or steps (e), (g), (i) and (j) are repeated one or more times, and the detectable change is observed.

391. The method of Claim 384 wherein the substrate is a transparent substrate or an opaque white substrate.

392. The method of Claim 391 wherein the detectable change is the formation of dark areas on the substrate.

393. The method of Claim 384 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

394. The method of Claim 393 wherein the nanoparticles are made of gold or silver.

395. The method of Claim 384 wherein the substrate has a plurality of types of oligonucleotides attached to it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

396. The method of Claim 384 wherein the substrate is contacted with silver stain to produce the detectable change.

397. The method of Claim 395 wherein the substrate is contacted with silver stain to produce the detectable change.

398. The method of Claim 384 wherein the detectable change is observed with an optical scanner

399. The method of Claim 398 wherein the device is a flatbed scanner.

400. The method of Claim 398 wherein the scanner is linked to a computer loaded with software capable of calculating greyscale measurements, and the greyscale measurements are calculated. to provide a quantitative measure of the amount of nucleic acid detected.

401. The method of Claim 384 wherein the oligonucleotides attached to the substrate are located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

402. The method of Claim 401 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

403. The method of Claim 401 wherein the substrate is contacted with silver stain to produce the change in conductivity.

404. The method of Claim 397 wherein each of the plurality of oligonucleotides attached to the substrate in the array is located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

405. The method of Claim 404 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

406. The method of Claim 404 wherein the substrate is contacted with silver stain to produce the change in conductivity.

422. (Amended) A kit comprising a container holding nanoparticles according to any one of Claims 243[-265] or 253.

426. (Amended) A method of nanofabrication comprising  
providing at least one type of linking oligonucleotide having a selected sequence,  
the sequence of each type of linking oligonucleotide having at least two portions;

providing one or more types of nanoparticles according to any one of Claims 243 or 253, the recognition oligonucleotides on each of the types of nanoparticles comprising a sequence complementary to the sequence of a portion of a linking oligonucleotide; and

contacting the linking oligonucleotides and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles to the linking oligonucleotides so that a desired nanomaterial or nanostructure is formed wherein the nanoparticles are held together by oligonucleotide connectors.

b) 428. (Amended) A method of nanofabrication comprising:  
providing at least two types of nanoparticles according to any one of Claims 243 or 253,

could the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to that of the oligonucleotides on the second of the nanoparticles;

the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to that of the oligonucleotides on the first type of nanoparticles; and

contacting the first and second types of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles to each other so that a desired nanomaterial or nanostructure is formed.

430. (Amended) ~~Nanomaterials~~ or nanostructures composed of nanoparticles according to any one of Claims ~~243~~ or 253, the nanoparticles being held together by oligonucleotide connectors.

432. (Amended) A method of separating a selected nucleic acid having at least two portions from other nucleic acids, the method comprising:

providing two or more types of nanoparticles according to any one of Claims 243 or 253, the oligonucleotides on each of the types of nanoparticles having a sequence complementary to the sequence of one of the portions of the selected nucleic acid; and

contacting the nucleic acids and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the selected nucleic acid so that the nanoparticles hybridized to the selected nucleic acid aggregate and precipitate.

433. The nanoparticles according to any one of claims 243 or 253, wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

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434. The nanoparticles according to claim 433, wherein the salt solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides for each other.

435. The nanoparticles of Claim 433 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

436. The nanoparticles of Claim 435 wherein the nanoparticles are gold nanoparticles.

437. The nanoparticles of Claim 436 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

438. The nanoparticles of Claim 433 wherein all of the salt is added to the water in a single addition.

439. The nanoparticles of Claim 433 wherein the salt is added gradually over time.

440. The nanoparticles of Claim 433 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

441. The nanoparticles of Claim 440 wherein the salt is sodium chloride in a phosphate buffer.

442. The nanoparticles of Claim 433 wherein the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm<sup>2</sup>.

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cancel  
443. The nanoparticles of Claim 442 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm<sup>2</sup>.

444. The nanoparticles of Claim 443 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm<sup>2</sup> to about 40 picomoles/cm<sup>2</sup>.

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